# HERC Coverage Guidance – Vertebroplasty, Kyphoplasty, Sacroplasty
# Disposition of Public Comments

## General Comments

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| *American Association of Orthopaedic Surgeons* Washington, D.C | 1 | Thank you for the opportunity to comment on the draft guidance regarding vertebroplasty, kyphoplasty, and sacroplasty for routine osteoporotic compression fractures. The American Association of Orthopaedic Surgeons represents 98% of the orthopaedic surgeons practicing in the United States, 368 of who practice in Oregon. Orthopaedic surgeons are the preeminent physicians providing surgical treatment for musculoskeletal conditions and disease. I currently serve as the President of the AAOS and have practiced in Tualatin, Oregon for more than 30 years. | Thank you for taking the time to comment. |
| | 2 | The AAOS firmly supports the incorporation of evidence into clinical practice, and is actively involved in developing and promoting Evidence Based Clinical Practice Guidelines for a number of musculoskeletal conditions, including The Treatment of Symptomatic Osteoporotic Spinal Compression fractures (http://www.aaos.org/research/guidelines/SCFguideline.pdf), for which the corresponding Summary of Recommendations is attached. | Thank you for providing this reference. The HTAS appreciates the AAOS' interest in producing evidence-based practice guidelines, and is impressed by the rigor of your development process. |
| | 3 | Through the AAOS' rigorously researched evidence-based clinical practice guideline development process, the AAOS has determined that the three procedures addressed in your draft coverage guidance are distinct from each other and deserving of similarly distinct treatment in terms of coverage guidance. Recommendation 8 of the AAOS clinical practice guideline recommends "against vertebroplasty for patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms and who are neurologically intact" (Grade of Recommendation: A). The Oregon Draft Coverage Guidance is consistent with this recommendation. | The HTAS agrees. |
| | 4 | However, Recommendation 9 of the AAOS clinical practice guideline states that "kyphoplasty is an option for patients who present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms and who are neurologically intact" (Grade of Recommendation: C). The Oregon Draft Coverage Guidance is inconsistent with this recommendation. | The AAOS guideline relied on 5 studies, 4 of which were included in the WA HTA review, while an updated publication of the fifth trial was included in the WA HTA. Two compared kyphoplasty to conservative treatment and 3 compared it to vertebroplasty. The 2 trials that used conservative treatment as the comparator found clinically important differences only at 1 week and 1 month in one trial, and "possibly clinically important improvement" in the other. Two of the 3 trials that used vertebroplasty as the comparator found no difference between groups, while the third found differences in |

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| | | | favor of kyphoplasty only at 2 years. Because of the inconsistent results noted here, the AOSS downgraded the strength of their recommendation from moderate to weak, so that kyphoplasty could be an "option." |
| | 5 | The AAOS clinical practice guideline for The Treatment of Symptomatic Osteoporotic Spinal Compression Fractures does not address sacroplasty. The treatment of vertebral compression fractures by either kyphoplasty or vertebroplasty should be considered completely separately from sacroplasty for sacral insufficiency fractures, as these are distinct anatomical and pathologic conditions. | The HTAS appreciates this distinction but has chosen to address all three procedures in one guidance to reflect the scope of the evidence source. Although they are included in the same Coverage Guidance, each procedure is evaluated and recommendations are made separately. |
| | 6 | Given the distinctions between the three procedures and their evidence-based clinical practice guideline recommendations, the AAOS urges the HERC to consider amending its coverage guidance to be consistent with evidence-based clinical practice guidelines. This would mean amending the coverage guidance to read: "Vertebroplasty should not be covered for routine osteoporotic compression fractures. Kyphoplasty should be covered for routine osteoporotic compression fractures."<br>Thank you for your consideration of these amendments. | The HTAS understands the rationale presented but does not believe the evidence pertaining to kyphoplasty is sufficiently strong to recommend coverage of the procedure. |
| *Medtronic, Inc.*<br>Memphis, TN | 7 | We appreciate this opportunity to submit comments on the Health Technology Assessment Subcommittee's (HTAS) Draft Coverage Guidance for Vertebroplasty, Kyphoplasty and Sacroplasty. As you are aware, Medtronic's Spinal and Biologics division manufactures products that treat a variety of disorders of the spine. These products are utilized by spinal and orthopedic surgeons to treat patients with acute symptomatic vertebral compression fractures that are known to significantly impair quality of life and increase risk of death. We are very interested in ensuring that the coverage guidance for Kyphoplasty reflects the latest clinical evidence and standard of care. | Thank you for your comment and for providing the studies referred to in your comments. |
| | 8 | Thank you for the consideration of our previous comments submitted April 16, 2012. We applaud the HTAS decision to provide expanded coverage from the initial draft for balloon kyphoplasty (BKP), including coverage for all cancer indications and for non-routine osteoporotic compression fractures. We believe the clinical evidence clearly supports this determination. **Additionally, we believe that the evidence supports an even broader coverage determination and application for osteoporosis cases.** Recent evidence has emerged since the Washington Health Technology Assessment Program (WA HTAP) conducted their review that supports a broadened positive coverage determination. In addition, it is worth noting that the major commercial payers in Oregon, plus a Medicare Local Coverage Decision (LCD) for the Oregon region, | The HTAS makes its decisions based on evidence of effectiveness and harms, not on the basis of other payers' coverage policies. |

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| | | provide for a broader coverage of BKP. We ask the HTAS to adopt coverage guidance in keeping with the clinical indications of the LCD to expand coverage for patients with osteoporosis. | |
| | 9 | First, we submit the following as additional support of the HTAS positive coverage determination for BKP for all cancer indications. The growing body of evidence, including one randomized-controlled trial and two recent systematic reviews, demonstrates the relative superior safety and effectiveness of BKP compared to non-surgical management in the treatment of eligible vertebral compression fractures (VCFs) in patients with multiple myeloma or spinal metastases from primary tumors (Berenson 2011, Bouza 2009, Aghayev 2011). In addition, the National Institute for Health and Clinical Excellence (NICE, 2008) guidelines recommend cemental augmentation procedures for VCFs in cancer patients. | The search dates of the Bouza SR are included in the WA HTA review. The Aghayev review is narrative, not systematic. The Berenson RCT compared kyphoplasty to medical management in patients with malignancy, N=134, unblinded and funded by industry. Found significant decrease in pain in the KP group at 1 month. General NICE guidance for VP and KP due Dec 2012. |
| | 10 | Second, we appreciate and understand the HTAS evidence source as the WA HTAP, however, the Washington review was conducted in 2010 and relevant evidence has since emerged and should be considered as part of the HERC review. Discussion at the HTAS meeting on April 23, 2012 led to restrictions on coverage of osteoporosis cases partially because it was determined there were no long-term results regarding effectiveness. **However, studies are now available associating BKP with long-term effectiveness, increased life expectancy, and cost-effectiveness.** The final coverage guidance should reflect the latest clinical evidence and be expanded to include coverage for additional osteoporosis cases.<br>The following randomized, controlled trials indicate that BKP has been shown to provide clinically and statistically greater pain relief, restoration of mobility, and quality of life than non-surgical management (Boonen 2011, Berenson 2011). Please see our previous correspondence where we included more detailed explanations of the studies; the studies are also attached for your review | See Comment #9 concerning Berenson. Boonen is an unblinded RCT, N=300, funded by industry. Found improved SF-36 scores averaged across 24 months compared to non-surgical management, as well as pain and function scores at 1,3,6 and 12 mos. 23% drop out rate. Excluded fractures associated with malignancy or acute trauma. |
| | 11 | The following recent retrospective analysis of Medicare data indicates that BKP has been associated with an increased life expectancy compared to non-surgical management (Edidin OI 2012). In another analysis of Medicare patients published this year, BKP was determined cost-effective compared with non-surgical management (Edidin CEA 2012). Both of these studies showing the advantages of BKP should be considered as part of the HERC review. | These are both retrospective database studies that use a model for estimating life expectancy, not actual data, as well as claims data to identify vertebral fractures and their treatment. Both are highly susceptible to bias. |
| | 12 | Lastly, as further support for our assertion that the coverage for BKP ought to be extended for additional osteoporosis cases, we submit the results of our review of the coverage polices of the top ten commercial carriers in Oregon (the majority of which were updated in 2011, after the WA HTAP review). Eight of the ten carriers publish their policies and all of them have positive coverage policies for BKP for osteoporosis cases. Judging from information gathered from provider bulletins, it is likely the remaining two do as well. **Additionally, the Medicare LCD is positive for all indications for BKP.** | The HTAS makes its decisions based on evidence of effectiveness and harms, not on the basis of other payers' coverage policies.<br><br>Medicare LCD language confirmed. Entire |

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| | | Following are the indications for the Medicare LCD:<br>For Both Percutaneous Vertebroplasty and Percutaneous Vertebral Augmentation: One indication – painful compression fracture, regardless of etiology, described below.<br>Clearly demonstrated vertebral compression fracture, with severe pain, refractory to conservative treatment and referable specifically to that site – non-specific documentation of "lower back pain" or similar language will not support payment.<br>…<br>Neither Percutaneous Vertebroplasty nor Percutaneous Vertebral Augmentation is indicated for treatment of lesions of the sacrum or coccyx. NAS will not allow payment for any such treatment until and unless either becomes listed as a covered indication in FDA labeling AND literature supports and describes appropriate criteria for such use. The CPT Category III codes, 0200T and 0201T, are non-covered.<br>See: http://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=32032&ContrId=243&ver=11&ContrVer=1&CntrctrSelected=243*1&Cntrctr=243&name=Noridian+Administrative+Services%2c+LLC+(02301%2c+MAC+-+Part+A)&LCntrctr=243*1%7c244*1&bc=AgACAAIAAAAA&<br>To reduce confusion for surgeons and patients, we encourage the HTAS to adopt a final coverage guidance for BKP in keeping with the indications provided in the LCD. | policy is lengthy and included as a separate document. |
| | 13 | In summary, we applaud the work of the HTAS thus far on the draft coverage for BKP for all cancer indications and for non-routine osteoporotic compression fractures. However, it is our belief that the recent and emerging clinical evidence supports a broader application of coverage for BKP for other osteoporosis cases. It associates BKP with long-term positive outcomes, increased life expectancy and cost-effectiveness. We hope the HTAS will choose to follow the existing commercial policies and the indications of the LCD for the state of Oregon; they are supported by the new data showing positive results and long-term effectiveness for BKP in osteoporosis cases.<br>Thank you again for your consideration of our comments and the attached studies. | The provided studies do not substantially alter the conclusions of the WA HTA evidence report. |
| *DePuy Spine*<br>Raynham, MA | 14 | DePuy Spine Inc. is grateful for the opportunity to provide Oregon's Health Evidence Review Commission (HERC) with comments on its draft non-coverage policy for vertebroplasty, kyphoplasty, and sacroplasty for treatment of routine osteoporotic vertebral compression fractures (VCFs). We encourage the HERC to take into account the body of evidence for these treatment options, as well as feedback from the full spectrum of treating physicians (e.g., internists, interventional radiologists, pain specialists, and surgeons) and patients to ensure that its coverage policy fosters appropriate access to evidence-based treatment for VCFs.<br>Below we provide rationale for HERC's continued coverage of vertebroplasty and kyphoplasty for a | Thank you for your comment. |

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| | | carefully selected subset of patients with acute VCFs who fail to respond, or who are intolerant of, non-invasive management (NIM). | |
| | 15 | **Patients with debilitating symptoms despite an adequate trial of non-invasive management have few treatment options to reduce pain and hasten return to normal function after acute VCF.**<br>Few treatment options are available for patients suffering from painful VCFs that are unresponsive to non-invasive management (e.g., bed rest, physical therapy, analgesia, and bracing). As a result, patients may endure months of severe pain, restricted mobility, poor quality of life (QoL), and/or depression.[1] Patients with VCFs are confined to bed nine times more often than those without VCFs, increasing their risk of further VCFs and suboptimal recovery.[2] The impact of VCFs on QoL has been estimated to be similar to that attributable to chronic obstructive pulmonary disease.[3] | HTAS understands the significant impact of VCFs on patients. |
| | 16 | **The two sham-controlled studies published in the NEJM fail to provide evidence about the role of vertebroplasty for a carefully selected subgroup of patients with acute VCFs.**<br>Randomized controlled clinical trials (RCTs) that compared vertebroplasty to a simulated procedure (sham) highlight the challenges of conducting adequately powered RCTs of vertebroplasty, including barriers to recruitment and the need for careful patient selection.[4, 5] Subsequent to the publication of these studies in the New England Journal of Medicine (NEJM), position statements by national medical societies identified severe limitations that pose challenges to interpretation of these studies.[6, 7] Among these, high non-participation rates, the inclusion of patients with chronic fractures, measurement of "overall pain" rather than back pain, significant crossover from NIM, potential analgesic effect from peri-facet injection, as well as limited statistical power warrant particular concern. Further, the studies' investigators did not require clinical correlation of fracture level/imaging with physical examination (percussion, palpation, motion testing), which is particularly important for verification of symptomatic VCFs in elderly patients. Taken together, these issues limit the generalizability and validity of the studies for real-world clinical management of VCFs.<br>In order to address these limitations and generate new evidence for a relevant sub-population of patients with VCFs, investigators currently are recruiting patients to participate in VERTOS IV, which will compare vertebroplasty to sham procedure among patients with radiographically confirmed acute VCFs (≤ 6 weeks of pain).[8] | While there may be issues related to generalizability of the two sham controlled trials, they offer the best evidence regarding effectiveness. See also response to comment #27 |
| | 17 | **Two published, randomized studies were powered to evaluate the safety and efficacy of kyphoplasty and vertebroplasty relative to NIM for the subset of patients with acute VCFs.**<br>Prospective, randomized controlled studies that compared either vertebroplasty or kyphoplasty to NIM have shown these treatments to provide benefits in the way of improved pain relief and/or function relative to non-surgical management for well-defined population of patients with acute, non-malignant VCFs. In the randomized Fracture Reduction Evaluation (FREE) study, statistically significant improvements | The citations listed were published before the date of the WA HTA report (Aug 2010). The HTAS bases their guidance documents on reviews of the literature that utilize the highest standards of evidence based medicine. Studies are included or excluded |

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| | | in pain and function were sustained at 12 months for patients receiving kyphoplasty versus NIM.[9] In VERTOS II, a prospective multicenter RCT with 202 patients with acute VCFs, vertebroplasty provided statistically significant improvements in pain relief versus NIM at 12 months post-procedure (VAS 2.2 vs. 3.8; p = 0.014).[10] The incidence of new fractures was similar in both groups at the one-year follow-up time point (p = 0.28), and there were no serious complications or adverse events. Unlike the studies of vertebroplasty versus sham procedures, these two studies provide direct evidence for a well-defined population of patients suffering from acute VCFs (i.e., fractures ≤ 3 months of age), but cannot rule out response bias that may have occurred due to lack of blinding. | based on transparent, reproducible criteria; therefore the HTAS does not investigate individual studies. The HTAS assumes that the conclusions reached by the authors of these reviews weigh all the available evidence in accordance with the principles of evidence based medicine, and does not attempt to re-review the entire body of evidence to reach its own conclusions. |
| | 18 | **Professional guidelines on the appropriateness of vertebroplasty and kyphoplasty are varied and informed by distinct evidence.**<br>Two professional guidelines were published *prior to availability* of the aforementioned VERTOS II study, which established the relative efficacy of vertebroplasty compared with NIM for acute VCFs. The American Academy of Orthopaedic Surgeons (AAOS) in 2010 released guidelines that vertebroplasty should not be considered for treatment of VCFs, a decision heavily influenced by the aforementioned sham-controlled studies.[11] In contrast, Appropriateness Criteria® published by the American College of Radiology (ACR) in 2010 indicate that both vertebroplasty and kyphoplasty may be appropriate for carefully selected patients after a failed trial of conservative measures or due to intolerance to conservative management.[12] The following vignettes within the ACR's Appropriateness Criteria® describe patients who may be considered for vertebroplasty or kyphoplasty after failure, or intolerance of, narcotics or non-steroidal anti-inflammatory drugs (NSAIDS):<br>*"75-year-old woman with a documented old T9 compression fracture and 1-3-week old painful compression fracture of T12 without history of trauma. Patient has a history of gastric ulcer-related NSAIDs 2 years ago. Patient lives alone, is active, and the new fracture is impeding her independence. The older T9 fracture healed within 4-5 weeks."*<br>*"80-year-old woman with a documented old T9 compression fracture treated by a percutaneous vertebroplasty 4 months ago. Now complains of a 5-week-old painful compression fracture of T12 without history of trauma. Patient is chronically constipated with history of cathartic abuse. Patient lives alone, is active, and the new fracture is impeding her independence."* | While the AAOS literature search was completed prior to the publication of VERTOS II, the WA HTA report was not, and VERTOS II was included in that review. |
| | 19 | **The HERC's coverage decision should be informed by the full body of literature, including new clinical studies published since completion of Washington State Healthcare Authority's systematic review.**<br>The Washington State Healthcare Authority's coverage decision was based on an analysis dated November 4, 2010, suggesting that an updated systematic review of the literature is warranted. For example, two prospective, randomized studies comparing vertebroplasty to NIM for patients with acute (≤ 3 months) | Thank you for providing this reference. This unblinded study does not negate the findings of the two sham trials that had more appropriate control groups and found no differences in outcomes. |

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| | | and chronic (> 3 months) non-neoplastic VCFs were not yet published at the time of the Washington State HTA, and should be included in the HERC's review.[13, 14] Farrokhi et al. (2011) randomized patients to receive either vertebroplasty (n = 40) or NIM (n = 42).[13] Pain relief in the vertebroplasty group was significantly greater than that in the NIM group at 1 week, 2 months and 6 months ($p<0.05$), demonstrating an immediate and sustained benefit from vertebroplasty. Pain relief was maintained for the 36-month study duration, though between-group differences were not statistically significant beyond 12 months. Improvements in disability as measured by the Oswestry Disability Index (ODI) were statistically greater at all time points (1 week to 36 months) for patients in the vertebroplasty group relative to those in the NIM group. The incidence of new vertebral fractures was statistically higher among patients in the NIM arm relative to those in the vertebroplasty arm (13.3% versus 2.2%, $p < 0.01$). One patient who received vertebroplasty experienced cement leakage that resulted in lower-extremity pain and weakness subsequently alleviated with spinal decompression surgery. | |
| | 20 | In a single-center study in Spain, Blasco and colleagues randomized 125 patients to receive either vertebroplasty or NIM.[14] Patients in both treatment arms experienced reduced pain at all time points through 12-month follow up, though those in the vertebroplasty arm experienced superior improvement at the 2-month time point ($p = 0.035$). Significant improvement from baseline function, as measured by the Quality of Life Questionnaire of the European Foundation for Osteoporosis [Qualeffo-41] was observed at all time points for patients in the vertebroplasty arm and only at the 6-month time point for patients who received NIM. Vertebroplasty was associated with a significantly increased incidence of vertebral fractures (odds ratio [OR], 2.78; 95% confidence interval [CI], 1.02–7.62). Cement leakage occurred in 49% of vertebroplasty procedures, though these were not associated with immediate clinical sequelae. | Thank you for providing this reference. This unblinded study does not negate the findings of the two sham trials that had more appropriate control groups and found no differences in outcomes. |
| | 21 | A recently completed meta-analysis completed by Papanastassiou et al. (2012) sought to determine if differences in safety or efficacy exist between balloon kyphoplasty, vertebroplasty, and NIM for the treatment of VCFs.[15] A total of 27 studies were included, 9 of which compared vertebroplasty to NIM, 12 of which compared balloon kyphoplasty to vertebroplasty, and 6 of which compared balloon kyphoplasty to NIM. Key findings from that study are as follows:<br>• Pain reduction for both kyphoplasty (-5.07/10 points) and vertebroplasty (-4.55/10) was statistically superior ($p < 0.01$) to that for NIM (-2.17/10), while no difference was found between kyphoplasty and vertebroplasty ($p = 0.35$).<br>• Subsequent fractures occurred more frequently in the NIM group (22 %) compared with vertebroplasty (11 %, $p = 0.04$) and kyphoplasty (11 %, $p = 0.01$).<br>• Patients with baseline fracture age less than 7 weeks experienced greater pain reduction (approximately 5.0 to 7.0 points) than those with VCFs treated later (approximately 2.3 to 4.5 points). | Based on this MA, KP appears to have similar efficacy to VP. Since VP does not have evidence of effectiveness compared to sham, one could conclude that KP similarly offers no benefit compared to sham. |

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| | | • Improvements QoL, as measured by the SF-36 Physical Component Summary (PCS) were superior for kyphoplasty versus vertebroplasty (p = 0.04), though the study's authors note that these differences should be interpreted with caution due to a limited number of studies and heterogeneity of pooled results. | |
| | 22 | **The HERC should seek to minimize variation to patient access to vertebroplasty and kyphoplasty in the state of Oregon and, like other public and private payers in the state, preserve access for the subset of refractory patients most likely to benefit from these procedures.**<br>In 2011, Noridian Administrative Services (NAS), the Medicare Administrative Contractor (MAC) for Oregon and nine other states, released a coverage policy that provides access to vertebroplasty and kyphoplasty for a limited subgroup of patients suffering from acute VCF.[16] The following are among key coverage criteria in this policy, as informed by the full-body of literature and extensive public comment:<br>• Vertebral compression fracture (VCF), with severe pain, refractory to conservative treatment and referable specifically to that site;<br>• Patient's pain is documented to be severe (e.g., 7 or greater on 0 to 10 Visual Analog Scale [VAS]);<br>• Fracture has been acceptably confirmed by plain film x-ray or by MRI, and results correlate unequivocally with the patient's pain; and<br>• Fracture has been present for 4 months or less. | The HTAS makes its decisions based on evidence of effectiveness and harms, not on the basis of other payers' coverage policies.<br><br>Limitations listed by the commenter confirmed in the LCD.<br><br>Addition of the definition of when a compression fracture is not routine adds additional specificity. It is similar to the NAS coverage policy. |
| | 23 | DePuy Spine supports access to vertebroplasty and kyphoplasty for patients who are refractory to conservative medical management and who have met other professional society criteria. We encourage HERC's final coverage position to thoughtfully reflect the body of literature in its totality, including professional society treatment guidelines, Medicare and commercial payer policies, and not least the perspectives of patients in the state of Oregon. | HTAS does not find that the evidence supports the effectiveness of either of these procedures. |
| *North American Spine Society*<br>Burr Ridge, IL | 24 | The North American Spine Society would like to take this opportunity to comment on the recently proposed draft coverage guidance from Oregon Health Evidence Review Commission (HERC) to revise their current coverage guidance for vertebral augmentation for osteoporotic compression and sacral fractures. NASS is a multispecialty medical organization dedicated to fostering the highest quality, evidence-based, ethical spine care. | Thank you for this information and for taking the time to comment. In the future, please provide full citations for studies referenced in your comments. |
| | 25 | In reviewing the draft coverage guidance, we recognize that HERC has modified the Washington State Health Care Authority Health Technology Assessment (HTA) for Vertebroplasty, Kyphoplasty and Sacroplasty that was published in 2010.<br>NASS has provided comments previously on Vertebroplasty, Kyphoplasty and Sacroplasty to Washington State HTA on February 18, 2011 and Noridian on May 27, 2011. | Thank you for this information. |
| | 26 | NASS believes there should be several distinctions made when considering kyphoplasty, vertebroplasty | The HTAS appreciates this distinction but |

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| | | and sacroplasty. The treatment of vertebral compression fractures by either kyphoplasty or vertebroplasty should be considered completely separately from sacroplasty for sacral insufficiency fractures. These are distinct anatomical and pathologic conditions. It is also imperative to distinguish cement augmentation procedures for neoplasm either primary or metastatic as a distinct and separate entity from osteoporotic compression fractures. | has chosen to address all three procedures in one guidance to reflect the scope of the evidence source. Although they are included in the same Coverage Guidance, each procedure is evaluated and recommendations are made separately. |
| | 27 | Within the comment letters to Washington State HTA and Noridian, we discussed the relevance of data published subsequent to the two New England Journal of Medicine (NEJM) articles (i.e. Kallmes et al, Buchbinder et al). NASS disagrees with the distinction in coverage policy between vertebroplasty and kyphoplasty. We certainly appreciate the decision to limit coverage of vertebroplasty based on the recent randomized controlled trials by Buchbinder et al and Kallmes et al published in the New England Journal of Medicine. However, these studies have legitimate weaknesses, particularly in the acuity of the fractures. NASS has published a systematic response to these two studies recently and appreciate the investigators' responses to our critique. Most notably, the two studies do not provide irrefutable evidence that vertebroplasty would not result in better outcomes compared to a sham procedure in truly acute fractures (i.e. 3 months old or less). | Citations not provided, but retrieved.<br>Stated weaknesses include:<br>• inclusion criteria included medical therapy for at least 4 weeks, resulting in a study of "healed fractures"<br>• small enrollment (30-36% of eligible patients), limiting subgroup analysis<br>• exclusion of patients with pathologic fractures<br>• sham local anaesthetic injection is not an appropriate control<br>• difference in cross over rates<br>Authors responded to all of these weaknesses.<br>It is not clear why the commenter makes the assumption that these two trials do not address acute fractures. In the Kallmes trial, patients could have pain for up to a year, but 38-44% had pain for 1-13 weeks, and for fractures of an uncertain age, marrow edema was required. In the Buchbinder trial, marrow edema was also required, and 32% of patients had pain duration less than 6 weeks. |
| | 28 | Second, the treatment effects in the NEJM studies about vertebroplasty were comparable to those found in the randomized controlled trials about kyphoplasty. Considering the inherent similarity of the two procedures, NASS believes that the same coverage rationale for kyphoplasty should be applied to vertebroplasty. The strongest support for this statement is the fact that kyphoplasty has been directly | HTAS agrees that the inherent similarity of KP and VP allows similar coverage decisions to be made. However, since VP does not have evidence of effectiveness compared |

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| | | compared to non-operative treatment in a randomized trial, while vertebroplasty was not compared to non-operative treatment in the NEJM trials. Thus, there is a lack of evidence of the comparative effectiveness of the non-operative treatment prescribed in the current draft policy versus vertebroplasty. Previous prospective, nonrandomized evidence (Alvarez et al, 2006) suggests that vertebroplasty has advantages when performed within 6 weeks from fracture. | to sham, which is a study type that is less susceptible to bias, HTAS concludes that KP also does not have evidence of effectiveness.<br>In addition, the Kallmes and Buchbinder trials are supported by the findings of an open randomized trial that did not show any benefit of vertebroplasty over usual care at 3 months (Rousing 2009). See comment #52 for description of study. |
| | 29 | More recently, the study published by Klazen et al (Lancet, 2010), a randomized prospective study comparing vertebroplasty to non-operative treatment, demonstrated significantly better results with the former. Inherent in its design, this study was not blinded, and thus can be critiqued in this regard in comparison to the blinded, sham experiments published in the NEJM. Relevant to the current discussion, this study augments the current knowledge about the efficacy/effectiveness of vertebroplasty for osteoporotic compression fractures. | This unblinded study does not negate the findings of the two sham trials that had more appropriate control groups and found no differences in outcomes. |
| | 30 | 1. By using a non-operative treatment comparator, the study is more of a “real world” comparison of the two commonly used treatments, instead of the sham procedure used in the NEJM articles that included an anesthetic injection that may have some therapeutic effect. | Pain is an outcome that is highly subjective and susceptible to placebo effect. Use of a sham procedure is essential in this circumstance to identify true effect. |
| | 31 | 2. The initial enrollment process detailed that 229 patients who could have been included in the study had spontaneous resolution of their pain and thus dropped out. This reinforces previously known knowledge about the favorable natural history of most patients with acute osteoporotic compression fractures. | This supports the rationale of the Kallmes and Buchbinder trials to require 4 weeks of medical therapy before enrollment. |
| | 32 | 3. The inclusion criteria were much more stringent and specific than those used in the two NEJM studies, specifically that patients had a “visual analogue scale [pain] score of 5 or more; bone oedema of vertebral fracture on MRI; focal tenderness at fracture level…” prior to entry. | The significance of this fact, as it pertains to this evidence, is not clear. |
| | 33 | 4. Fractures, on average, were more acute in the Klazen et al study compared to the NEJM studies. | The significance of this fact, as it pertains to this evidence, is not clear. |
| | 34 | At the NASS 26th Annual Meeting, November 2011 in Chicago IL, there were presentations showing both better hospital discharge outcomes and better survivorship in patients treated with vertebral cement augmentation. Edidin et al (Spine Journal 2011) looked at life expectancy following diagnosis of a vertebral compression fracture. The study utilized the Medicare database and looked at 100 percent of national inpatient and outpatient claims data from 2005–2008 for patients with a newly diagnosed vertebral compression fracture (VCF) identified using ICD-9-CM diagnosis codes. Using CPT-4 and ICD-9-CM | Both of these are retrospective database studies that are highly susceptible to bias. Gerling citation not provided. |

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| | | procedure codes, patients were stratified into operated (kyphoplasty or vertebroplasty) and non-operated patients. Of the 858,978 patients with a newly diagnosed VCF were identified, including 119,253 kyphoplasty patients (13.9 percent) and 63,693 vertebroplasty patients (7.4 percent). Across all gender-age groups, the median life expectancy predicted by the parametric Weibull model was 2.2 to 7.3 years greater for operated than non-operated patients. Although in abstract form in The Spine Journal the results were published in the Journal of Bone and Mineral Research, 2011 Jul;26(7):1617-26. Gerling et al (Spine, 2011) in their review of Cement Augmentation of Refractory Osteoporotic Vertebral Compression Fractures came to similar conclusions. They reviewed a university hospital database to identify all participants treated with primary diagnosis of osteoporotic vertebral compression fracture between 1993 and 2006. They identified 46 patients treated with cement augmentation and 129 matched controls meeting inclusion criteria. Patients not differ with respect to age, sex, and comorbidities. "A significant survival advantage was found after cement augmentation compared with controls ($P < 0.001$; log rank), regardless of co-morbidities, age, or the number of fractures diagnosed at the start date ($P = 0.565$)." They concluded cement augmentation of refractory osteoporotic vertebral compression fracture improves survival for up to 2 years when compared with conservative pain management with bed rest, narcotics, and extension bracing, regardless of age, sex, and number of fractures or co morbidities. | |
| | 35 | Zambini et al (Spine Journal 2011) looked at hospital outcomes of both osteoporotic and neoplastic vertebral compression fracture treatment with kyphoplasty and vertebroplasty in the United States. The study utilized a national healthcare database, Nationwide Inpatient Sample (NIS), which is an annual survey of approximately 1,000 hospitals, containing data from 20 percent of all inpatient hospitalizations in the U.S. In a nationwide estimate of 86,810 neoplastic (74.7 percent emergent, 25.3 percent elective) and 370,933 non-neoplastic (77.5 percent emergent, 22.5 percent elective) patients were identified. Among the neoplastic group, 71.8 percent of elective and 23.0 percent of emergent patients underwent kyphoplasty, while for the non-neoplastic group, 69.4 percent of elective and 17.5 percent of emergent patients underwent kyphoplasty. The corresponding percent of patients that underwent vertebroplasty was 10.4 percent, 11.0 percent, 9.6 percent, and 9.0 percent, respectively. The remaining patients underwent non surgical management (NSM). After adjusting for all covariates, compared with NSM patients, kyphoplasty and vertebroplasty patients had significantly higher likelihood of routine discharge ($P > 0.001$) and lower risk of discharge to skilled nursing facility ($P > 0.001$). Compared with NSM patients, kyphoplasty and vertebroplasty patients also had lower risk of in-hospital mortality, pressure ulcer, pneumonia, and infection ($P > 0.029$), but had higher risk of complication of surgical procedure or medical care ($P > 0.001$). They concluded kyphoplasty and vertebroplasty patients have a higher likelihood of better in-hospital outcomes than NSM patients. These results while only currently in abstract form are compelling and NASS will continue to follow and review the final publication. | Database studies are considered a low level of evidence and highly susceptible to bias. Citation not provided. |
| | 36 | Considering the findings of the Lancet study, comparing them to those of the NEJM studies, in addition to | HTAS disagrees that the evidence supports |

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| | | previously published, non-industry sponsored prospective comparative data (Alvarez et al, 2006), a number of points become apparent.<br>1. Vertebral augmentation can be considered in patients with pain that persists beyond six weeks despite non-operative care. This is supported by previous data that has demonstrated spontaneous pain relief in the majority of patients in the acute setting in this approximate time interval. | this recommendation. |
| | 37 | 2. Vertebral augmentation via vertebroplasty or kyphoplasty should not be routinely considered in patients with fractures that are older than 3 months. This is supported by the findings of the two NEJM studies that failed to show that vertebroplasty was better than placebo in patients who mostly had fractures that were older than 3 months. | The NEJM studies also showed no effect on the 32-44% of patients who had fractures less than 3 months old. |
| | 38 | 3. Within the appropriate time interval (6 weeks to 3 months from the onset of fracture), vertebral augmentation should be considered only if the patient has an MRI (or bone scan) that demonstrates bone edema within the fractured vertebral body and that this level corresponds to the site of pain upon physical examination (i.e. via percussing or palpating the patient's spinous processes). This can be confirmed with a plain radiograph with an opaque marker placed at the point of maximal tenderness. | The Buchbinder trial required evidence of marrow edema in all participants, and the Kallmes trial required it for any fracture of uncertain age. Even so, there was no evidence of efficacy of VP. |
| | 39 | 4. Vertebral augmentation prior to six weeks should be considered only in those patients who are admitted to a hospital for management of pain associated with an osteoporotic compression fracture, are bed-bound secondary to pain, have failed to respond to non-operative inpatient care, and have satisfied the details outlined in criteria 3 (above). This is particularly true for patients with chemically-induced osteoporosis from medications such as corticosteroids or those with malignancy in whom bed rest could result in hypercalcemia. | The evidence does not support differential treatment based on the subgroups described by the commenter. |
| | 40 | 5. We do not feel that a unilateral non-coverage determination is appropriate. NASS believes it would be far better to enforce appropriateness criteria to coverage of this procedure. | With the addition of a definition of when a compression fracture is not routine, the guidance is no longer a "unilateral non-coverage determination". Coverage is allowed for non-routine fractures, which is similar to appropriateness criteria. |
| | 41 | 6. NASS currently agrees with a non-coverage policy for sacroplasty until further evidence is published. | Thank you for your comment. |
| | 42 | 7. We strongly feel that vertebral cement augmentation for the treatment of pathological fractures (i.e. metastatic lesions, multiple myeloma) should be covered as a medically necessary procedure. The coverage policy should distinguish between vertebral cement augmentation for osteoporotic compression fractures, which should follow the above described appropriateness criteria, and pathological fractures, which should not, by nature of the disease, have a restricted time period of appropriate use.<br>NASS hopes that you consider the above appropriate use criteria in development of a finalized policy for | HTAS did not include guidance on treatment of pathologic fractures due to limitations of the evidence base. |

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| | | vertebral augmentation. | |
| *Oregon Association of Orthopaedists, Inc.*<br>Portland, OR | 43 | The following comments are submitted on behalf of the Oregon Association of Orthopaedists, Inc., whose members practice throughout the state of Oregon. Additionally, I have practiced as a spine specialist in Oregon since 1988.<br>We want to endorse the recommendation submitted by the North American Spine Society (NASS) that your guidance should reflect the distinctions between kyphoplasty, vertebroplasty and sacroplasty. | Thank you for this information and for taking the time to comment. |
| | 44 | We concur with the NASS' clinical practice guideline recommending kyphoplasty or vertebroplasty treatment for patients who present with an osteoporotic spinal compression fracture with 6 weeks to 3 months of symptoms. This procedure is only indicated before 6 weeks if the patient is incapacitated and essentially at bed rest with the pain. There should also be MRI imaging showing acute changes with correlating clinical signs and symptoms and no neurologic deficit. For these patients, kyphoplasty and vertebroplasty can significantly relieve pain and restore mobility. The NASS May 22, 2012 letter clearly summarized an accurate review of the literature supporting this position. The Washington State Health Care Authority HTAA 2010 policy is based on a less rigorous critique of the literature. | The NASS letter does not represent a thorough review of the literature, since no systematic search was done. It is not clear why the commenter believes that the WA HTA policy, which was based on a systematic review of the literature, is less rigorous. |
| | 45 | Your draft guidance does not distinguish between vertebroplasty and kyphoplasty. We concur with NASS' recommendation that your coverage guidance be amended to read: “Vertebroplasty and Kyphoplasty should be covered for routine osteoporotic compression fractures."<br>The treatment of vertebral compression fractures by kyphoplasty or vertebroplasty is separate from sacroplasty for sacral insufficiency fractures.<br>Thank you for your consideration of our comments. | HTAS does not believe the evidence for VP and KP is sufficiently strong to recommend coverage.<br><br>HTAS appreciates the distinction between procedures but has chosen to address all three procedures in one guidance to reflect the scope of the evidence source. Although they are included in the same Coverage Guidance, each procedure is evaluated and recommendations are made separately. |
| *Society of Interventional Radiology*<br>Fairfax, VA | 46 | The Society of Interventional Radiology (SIR) appreciates the opportunity to present our opinion on the above-referenced topic.<br>The Society of Interventional Radiology (SIR) is a professional medical association that represents 5,000 members who are practicing in the specialty of vascular and interventional radiology. The Society is dedicated to improving public health through pioneering advances in minimally invasive, image-guided therapy. Our members are at the forefront of new and minimally invasive therapies to treat an array of diseases and conditions without surgery. Interventional radiology treatments have become first-line care for a wide variety of conditions and patients, including osteoporosis patients with spinal fractures, | Thank you for this information and for taking the time to comment. In the future, please provide full citations for studies referenced in your comments. (No citations were provided) |

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| | | peripheral arterial disease, deep vein thrombosis, uterine fibroids, cancer and stroke patients. | |
| | 47 | The draft guidance of the Health Evidence Review Commission has indicated that vertebroplasty, kyphoplasty, and sacroplasty should not be covered for routine osteoporotic compression fractures.<br>Although the HERC has made a clinical distinction between vertebroplasty and kyphoplasty, it is our opinion that for purposes of analysis, it is appropriate to consider these two procedures collectively. The clinical decision-making to diagnosis a vertebral compression fracture (VCF) is identical prior to either procedure, and patient outcomes for both procedures are similar. Therefore, in our analysis of the trials below, we will be considering kyphoplasty in addition to vertebroplasty together as treatment for osteoporotic vertebral fractures. In terms of sacroplasty, the SIR is actively working to coordinate research on this procedure, and although we are encouraged by the anecdotal reports, we concur that it should not be considered for routine fractures. | HTAS agrees that because of similarity of VP and KP procedures, considering the procedures together is reasonable. Since as the commenter states, "patient outcomes for both procedures are similar", and because the best evidence indicates the VP is not effective for osteoporotic VCFs, neither procedure should be covered. |
| | 48 | Within the past three years, results from five randomized controlled trials of percutaneous vertebral augmentation (PVA) vs. medical or sham therapy have been reported. The two largest trials totaling 502 patients reported better outcomes for patients treated with PVA vs. conservative medical therapy. Two smaller trials totaling 209 patients reported no improvement in outcomes vs. sham therapy. The smallest trial including 49 patients reported better outcomes at one month for patients treated with PVA vs. conservative therapy, but no improvement in outcomes at three or twelve months. The inclusion criteria, primary outcome measures, and results of each trial are briefly summarized below. | Please see disposition for individual trial summaries listed below. |
| | 49 | ***Trial Summaries:***<br>The *Fracture Reduction Evaluation (FREE*) trial enrolled 300 patients over a 34 months period. One thousand twelve hundred seventy-nine patients were assessed, of whom 614 met eligibility criteria and 300 (49%) were enrolled. Inclusion criteria included one to three VCF, at least one of which had edema demonstrated by MRI and >15% height loss, and fracture age < three months. Although patients with multiple myeloma or metastases were included; only two such patients were enrolled in each treatment arm, so that this was effectively a study of osteoporotic VCF. Kyphoplasties were performed upon 149 patients; the remaining 151 patients were treated with medical therapy. Follow up evaluation included both clinical and radiographic evaluations up to one year after treatment. The primary outcome measure was the change in the SF-36 physical component score from baseline at one month. The primary outcome measure was significantly greater for those patients treated with vertebral augmentation ($p<0.001$). Secondary outcome measures of back pain and disability showed consistently superior and statistically significant results for the vertebral augmentation group up to one year after treatment, with the exception of opiate use at 12 months, which was not significantly different between the two groups. This was an industry sponsored study.<br>In the FREE study, pain and narcotic use were also among several secondary outcomes. Graph showing | Citation not provided. This unblinded study does not negate the findings of the two sham trials that had more appropriate control groups and found no differences in outcomes. |

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| | | significant differences in narcotic use between intervention and control only at the 3 month assessment (no differences at 1 week, 1 month, 6 months and 1 year). Referenced as: *Ashraf, Unpublished Presentation, 2010* | |
| | 50 | The ***Investigational Vertebroplasty Safety and Efficacy Trial (INVEST***) trial by Kallmes, et al enrolled 131 patients over a 50 month period. The original enrollment target was 250 patients, which was revised downward. One thousand eight hundred thirteen patients were assessed, of whom 431 met eligibility criteria and 131 (30%) were enrolled. Inclusion criteria included one to three VCF and fracture age of < twelve months. Patients with known malignancy were excluded. Patients with VCF of uncertain age could be enrolled if an MRI showed edema or a bone scan showed hyperactive uptake. Vertebroplasties were performed upon 68 patients and sham procedures upon 63 patients. The sham procedure included superficial and deep injection of local anesthetics and mixing of cement within the operating room to simulate a vertebral augmentation procedure, as this was to be a blinded trial. Follow up consisted of interviews conducted in person at one and twelve months and by telephone at three and fourteen days and three months, and radiographs at twelve months. Physical reevaluation was not performed as part of the follow up protocol. The primary outcome measure was the change in the modified Roland-Morris Disability Questionnaire and average pain intensity at one month. The primary outcome measures were not significantly different between the two patient groups at one month. A secondary outcome measure was clinically meaningful improvement in pain at one month; 64% of patients receiving vertebral augmentation achieved this vs. 48% of controls (p=0.06). This outcome is particularly notable because the *p* value is so close to reaching statistical significance. Had the original enrollment target been met and with the same distributions of patient outcomes, this study would have shown statistically significant positive results for clinically meaningful pain improvement at one month for the vertebral augmentation arm. The SIR commented on this trial in detail in a letter to the *New England Journal of Medicine.* | The assumption that if the original enrollment target had been met, the study would have shown statistically significant positive results cannot be supported. The commenter assumes that VP patients would have more favorable outcomes. Of note, study groups did not differ significantly on ANY primary or secondary outcomes, including pain and QOL. While there was indeed a trend seen in clinically meaningful pain improvement in the VP group, no such trend was seen in physical disability related to back pain outcome (P=0.99). This study had 80% power to detect important differences in the primary outcome measures (a 3 point difference between groups on the Roland-Morris Disability Questionnaire, or a 1.5 point difference on patient rating of back pain intensity on a scale of 1-10). |
| | 51 | The randomized trial of vertebroplasty for painful osteoporotic fractures reported by Buchbinder et al enrolled 78 patients over a 54 month period. Four hundred sixty eight patients were assessed, of whom 219 met eligibility criteria and 78 (36%) were enrolled. Inclusion criteria included one or two VCF, fracture age of < twelve months, and MRI showing edema and/or a fracture line within the target vertebrae. Patients with known malignancy were excluded. Vertebroplasties were performed upon 38 patients and sham procedures upon 40 patients. The sham procedure was essentially the same as that used in the INVEST trial; this was also intended to be a blinded trial. Follow up consisted of mailed questionnaires at one week and one, three, and six months. As with the INVEST trial, physical reevaluation was not performed as part of the follow up protocol. The primary outcome measure was the score for overall pain over the course of the previous week at three months. The investigators reported that overall pain was not significantly different between patients undergoing vertebral augmentation and control subjects at any of the measured time points. This study was partially supported by industry. | Thank you for providing this study detail. Please provide citation in the future. |

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| | 52 | Rousing et al reported upon forty-nine patient treated with vertebroplasty or conservative therapy for osteoporotic VCF over a period of 84 months. The numbers of patients screened and assessed were not reported, so that the percentage of eligible patients enrolled remains unknown. Inclusion criteria included one to three VCF and fracture age < eight weeks. If more than one fracture was present, either edema on MRI or hyperactive uptake on a bone scan was used to determine which fractures were subacute. Forty patients were enrolled with pain of < two weeks duration. Patients with known malignancy were excluded. Vertebroplasties were performed upon 25 patients; the remaining 24 patients were treated with medical therapy. Follow up evaluation included both clinical and radiographic up to one year after treatment. The primary outcome measures were pain relief at three and twelve months as measured by the visual analog score (VAS). The investigators reported no statistically significant differences between the vertebral augmentation patients and the controls for pain or various functional measurements at three or twelve months. Supplementary analysis of pain at one month post treatment was, however, significantly different between the two groups; the mean VAS for the vertebral augmentation group (3.5) was significantly less than that for the controls (6.4) (p<0.01). | The outcome for which a significant effect was found (pain at 1 month) was not prespecified, and was not published in the original paper. Not clear if this is unpublished information, since no citation provided.<br>Of note, there was a significant increased risk of new VCFs in the intervention group (RR=2.9). |
| | 53 | ***VERTOS II***<br>On August 10, 2010, the results of the VERTOS II open-label randomized control trial were published online in *The Lancet.* VERTOS II provides markedly different results from Kallmes and Buchbinder.<br>The VERTOS II trial enrolled 202 patients over a 31 month period. Nine hundred thirty-four patients were screened, of whom 431 met eligibility criteria and 202 (47%) were enrolled. Inclusion criteria included one to three VCF, >15% vertebral height loss, bone edema on MRI, and fracture age of < six weeks. Patients with known malignancy were excluded. Vertebroplasties were performed upon 101 patients and the other 101 patients were treated with medical therapy. Follow up evaluation included both clinical and radiographic evaluations and patient questionnaires up to one year after treatment. The primary outcome measures were pain relief at one month and one year as measured by the visual analog score (VAS). Statistically significant improved pain relief was reported for patients treated with vertebral augmentation vs. controls at all measured time points from one day through one year. Secondary analyses included positive proof of cost-effectiveness for vertebral augmentation. This study was partially supported by industry. | Citation not provided. This unblinded study does not negate the findings of the two sham trials that had more appropriate control groups and found no differences in outcomes. |
| | 54 | In their findings, the VERTOS II authors note that vertebroplasty resulted in better pain relief after one, three, and six months and one year (*P*<0.001, *P*<0.001, *P*=0.025, and *P*=0.014, respectively) over conservative treatment. No serious complications or adverse events were reported. The incidence of new compression fractures was lower in the vertebroplasty group, although not significantly different from the conservative care (control) group. | Citation not provided. This unblinded study does not negate the findings of the two sham trials that had more appropriate control groups and found no differences in outcomes. |
| | 55 | The VERTOS II study additionally notes that vertebroplasty appears to be a cost effective treatment. The | Since evidence of effectiveness has not |

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| | | "adjusted trial-based incremental cost-effectiveness ratio for vertebroplasty, as compared to conservative treatment, was €22,685 per QALY gained." While we concur that many VCFs heal on their own through conservative treatment, the long term costs of conservative care, pain narcotics, risks of deep vein thrombosis, pressure sores, and often the need for skilled nursing (or extensive family care) are all potential consequences of conservative care. | been established, it is inappropriate to calculate an ICER. |
| | 56 | ***Analysis of the Trials***<br>Many controversial points were raised about the INVEST and Buchbinder et al trials that reported unexpectedly negative results. Whether a proper control arm for a vertebral augmentation study requires a sham procedure and whether such a sham procedure is ethical could be debated endlessly. Valid arguments can be made that either sham or medical treatment are acceptable and ethical controls. Whether appropriate follow up absolutely necessitates a physical examination might also be argued without resolution. The fragility of the statistics resulting from the INVEST trial's reduced enrollment has also been questioned. Debate continues about the alleged disparities between the patients enrolled into the INVEST, Buchbinder et al and Rousing et al trials vs. "real world" patients. None of these issues has any remaining significance now that data from all five trials has been published. Controversy and conflicting results permeate all aspects of medicine. One must focus upon both the quality and the quantity of evidence. | HTAS disagrees that controversy and conflicting results permeate all aspects of medicine, but agrees that when results are conflicting, is it imperative to focus on both the quality and the quantity of the evidence. |
| | 57 | The principle limitation of the VERTOS II study is the lack of a sham control. However, this deserves closer scrutiny. We in the medical provider community would comment that it is extremely difficult to recruit patients to a sham controlled trial, and it may not be feasible to conduct a study of this type. Of note, in the Kallmes study, many US institutions would not endorse sham trials and many investigators remain wary of sham trials. In fact, in recent presentations, Dr. Kallmes has stopped using the term sham for patients that receive medial branch block and has used the term "control intervention." | The lack of a sham control results in serious susceptibility to bias in this trial. Both sham controlled trials had sufficient power to detect a difference, and because they were completed, would seem to contradict the statement that such trials are not feasible. |
| | 58 | Therefore, the VERTOS II study represents the highest quality of data regarding percutaneous vertebroplasty for symptomatic vertebral compression fractures. The strength of this study is the on-going positive benefit at the one year follow up period. In addition to long term pain relief, this study demonstrated very rapid pain relief. Short term pain outcome is vitally important in and of itself as patients with disabling acute pain are at significant risk of further complications and are not candidates for long term conservative therapy. | HTAS disagrees that VERTOS II is the highest quality data. This was an unblinded study, which any evidence-based text book would identify as a lower quality of evidence than a blinded trial. |
| | 59 | ***Failed Conservative Treatment: What is the Threshold?***<br>In the treatment of an osteoporotic VCF, a common question that is confronted is how long should conservative medical management be employed before considering an interventional procedure? We would purport that assigning strict time limits to such a clinical decision would be problematic, and is best made on a case-by-case basis. The concept of a mandatory period of medical management prior to PVA | Defining a period for conservative treatment is not needed for procedures that are not effective. |

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| | | did not originate within the medical literature. The first published reference regarding this appears to be within an FDA guidance document published in 2004, "Clinical Trial Considerations: Vertebral Augmentation Devices to Treat Spinal Insufficiency Fractures". The document states that trials should include "patients that (sic) have failed various, currently available conservative treatments, after a sufficient time period when fractures would be expected to heal, generally eight weeks, or more." This document does not identify the author(s). The document has an expiration date of May 31, 2007, but has never been updated to our knowledge.<br>Accordingly, it is imperative that the decision to treat a VCF patient with a procedure must be made based on the presentation of each patient. As Klazen and her co-authors have speculated on the appropriateness of a medical management time period, they have also noted that "waiting 6 months in all patients can cause unnecessary pain and lost days for work and normal activity, when treatment with vertebral augmentation can provide almost immediate pain relief." | |
| | 60 | Defining what constitutes failure of conservative medical therapy for patients with VCF must integrate the patient's pain level, their response to analgesics, and their functional status including the impact of the medical therapies employed. Pain is, of course, subjective and individual, so that a certain level on a scale such as the VAS would be inadequate. However, pain that prevents ambulation or physical therapy represents a rather simple and dependable measure of both "severe" pain and significant disability. In addition, prompt restoration of ambulatory status or return to best prior sub-ambulatory status is clinically important. Even in the absence of other pathology, prolonged bed rest of greater than 48 hours duration clearly represents a significant hazard to the patient. For patients who were non –ambulatory prior to their incident VCF, a significant reduction in prior physical functional status should be considered the equivalent of being rendered non-ambulatory. | Defining a period for conservative treatment is not needed for procedures that are not effective. |
| | 61 | ***Summary:***<br>In sum, the two largest trials with the highest rates of patient enrollment and inclusion criteria generally viewed as being similar to typical "real world" patients have demonstrated benefits for vertebral augmentation persisting through one year post intervention. One of the smaller trials (Rousing et al) also demonstrated benefit from vertebral augmentation up to one month post intervention, but not beyond this point. The INVEST trial reported a very strong trend toward clinically meaningful improvement in pain for the vertebral augmentation group at one month. This finding narrowly missed achieving clinical significance despite the reduced number of patients enrolled vs. the original goal. Only the trial by Buchbinder et al failed to show that vertebral augmentation was beneficial at one month post intervention. A long-term (one year) benefit for vertebral augmentation was proven in the two largest trials; with total patient enrollment double that of the remaining three trials. Even if one were to accept the results from the INVEST and Buchbinder trials without question, a premise unacceptable to many | The two largest studies referred to by the commenter are unblinded, and of lower quality than the Kallmes and Buchbinder trials. HTAS disagrees that Buchbinder was the only trial to show lack of benefit at 1 month, since Kallmes found study groups did not differ significantly on ANY primary or secondary outcomes, including pain and QOL. It is not clear why unbiased physicians would have difficulty accepting the INVEST and Buchbinder trials, both published in the NEJM. |

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| | | physicians, the overall message remains clear. Therefore, after carefully weighing all of the available evidence, we must conclude that vertebral augmentation of osteoporotic VCF is very clearly beneficial in the short term and likely also in the long term, as well as being cost effective. | |
| | 62 | Prolonged arbitrary time periods of medical management do not have a role in the current treatment of patients with VCF. It is clear from the available clinical data that early intervention for patients severely affected by VCF produces better clinical outcomes and that this is also cost effective. | HTAS disagrees that early intervention with VP produces better clinical outcomes, since the available evidence does not support that conclusion. |
| | 63 | In sum, we would ask the HERC to carefully review all of the evidence, as well as to consider the professional opinions of physicians who are treating osteoporotic fracture patients every day. If denied access to spinal augmentation procedures, we believe that Oregonians would not have available to them a procedure that we believe should be part of a physician's treatment options.<br>I thank the HERC for the opportunity present our views. If desired, several of our members in Oregon would be pleased to go into further details about our position. | Thank you for your comment. HTAS has reached a different conclusion after examining the available evidence. |
| *Neurological Surgeon*<br>Portland, OR | 64 | The vertebroplasty/kyphoplasty topic is the most difficult of the three. The two randomized, controlled, blinded trials of vertebroplasty showed no advantage over sham surgery, but in fact, both groups were considerably better postoperatively. Therefore, some have interpreted the data not as showing that the procedure is ineffective, but showing that it works for reasons we do not understand. The Mayo Clinic is currently conducting further trials to try to determine why the sham surgery was so effective. There has also been much criticism of the methods of the studies. For example, the procedures were all done by radiologists, not spine surgeons, raising the question of whether the patients were properly screened for surgery, etc. Of course, criticizing and arguing against well done studies that show a result you do not want to see is sometimes inappropriate and must be viewed cautiously. | Thank you for this information, and for providing your perspective. |
| | 65 | My own practice is based on more than 8 years of experience with kyphoplasty. In over 100 procedures, I have found it to be about 80% effective in producing dramatic and rapid relief of pain. I have had a number of patients have 5 or more kyphoplasties over several years. I do not believe they would continue to undergo repeated procedures if the effect was not significant. Many patients have told me that they had to fail prolonged conservative management to get to their first kyphoplasty, so when they fractured another vertebra, they demanded immediate surgery without a waiting period, again indicating a strong belief in the effectiveness of the procedure. For patients hospitalized with unbearable pain, kyphoplasty has allowed mobilization and discharge, which must result in some cost savings over prolonged hospitalization or a nursing home. Many of these patients are in agony and without other effective treatment options. | Thank you for this information, and for providing your perspective. |
| | 66 | My own preference would be for the following:<br>1. Patients hospitalized because of unbearable pain from a new osteoporotic or malignant compression | Thank you for your comment. Definition of non-routine fracture matches your |

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| | | fracture and whose pain cannot be rapidly brought under control to the point of discharge to home should be allowed to have immediate kyphoplasty. | recommendation. |
| | 67 | 2. Patients with a new osteoporotic or malignant compression fracture who have failed 6-12 weeks of appropriate conservative management (pain medication, bracing, Miacalcin, TENS, PT, etc) with continuing need for potent narcotics, severe narcotic side effects (sedation, confusion, constipation, respiratory suppression), and/or impaired mobility should be allowed to have an elective kyphoplasty.<br><br>I realize that this is contrary to the draft recommendations, but I hope to allow some room for the procedure as some patients really do need more than medical management. | See comment #66. |